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EXAMINER

HUANG, EVELYN MEI

ART UNIT

PAPER NUMBER

1625

DATE MAILED: 09/30/2002

§

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/758,917

Applicant(s)

TEHIM ET AL.

Examiner

Evelyn Huang

Art Unit

1625

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-7 and 9-19 is/are pending in the application.
- 4a) Of the above claim(s) 14-19 is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-6 and 9-13 is/are rejected.
- 7) ☒ Claim(s) 7 is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). ____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) ____ 6) ☐ Other: ____

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1. Claims 1-7, 9-19 are pending. Claim 8 has been canceled according to the amendment filed on 7-12-2002.

Election/Restrictions

2. Newly submitted claims 14-19 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons:

This application, which is a continuation of PCT/CA97/00779, contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept.

- I. Claims 1-8, 10-13, drawn to a composition, a compound, and its method of use for inhibiting a neurotrophin-mediated activity.
- II. Claim 14, drawn to a method of treating pain.
- III. Claim 15, drawn to a method of treating Alzheimer's disease.
- IV. Claim 16, drawn to a method of treating epilepsy.
- V. Claim 17, drawn to a method of treating a neurological disease.
- VI. Claim 18, drawn to a method of treating neurological disease.
- VII. Claim 19, drawn to a method of repairing a nervous system injury.

Under PCT Rule 1.31 and 13.2 and 37 CFR 1.475, an international or a national stage application containing claims to different categories of invention will be considered to have unity of invention if the claims are drawn to one of the following combinations of categories:

- a. A product and a process especially adapted for the manufacture of the said product; or
- b. A product and a process of use of said product; or
- c. A product, a process specially adapted for the manufacture of the said product, and a use of the said product.

This application contains claims to more than one of the combinations of categories of invention set forth above since it contains 6 different alternative processes of use as described in

Group II to Group VII inventions, in addition to the inhibition of a neutrophin-mediated activity of Group I.

Since applicant has received an action on the merits for the originally presented invention of 'group I, claims 1-8, 10-13, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 14-19 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claim Rejections - 35 USC § 112(2)

3. The 112 second paragraph rejection is withdrawn in view of the amendment and applicant's remarks.

Claim Rejections - 35 USC § 102

4. The 35 U.S.C. 102(b) rejection over Costi is ***maintained*** for reasons of record. The pharmaceutical composition comprising compound 4ca (page 1012) is still encompassed by the instant amended claims.

5. The 35 U.S.C. 102(b) over Sestanji I (3821383, PTO-1449) is withdrawn because the amendment that the loweralkyl- R^5R^6 is $C_{2-4}alkylR^5R^6$ and the proviso that R^2 and R^3 are not both hydrogen have set a demarcation from the prior art compound.

6. The 35 U.S.C. 102(b) rejection over Malizia (EP 206322, PTO-1449) or Semenovich (DE 2521139, PTO-1449) is withdrawn because the amendment that the loweralkyl-(R^5)(R^6) is $C_{2-4}alkyl(R^5)(R^6)$ and the proviso that R^2 and R^3 are not both hydrogen have set a demarcation from the prior art compound.

7. The 35 U.S.C. 102(b) rejection over Sestanj II (4254109, PTO-1449) is withdrawn because the amendment that the loweralkyl- R^5R^6 is $C_{2-4}alkylR^5R^6$ and the proviso that R^2 and R^3 are not both hydrogen have set a demarcation from the prior art compound.

8. The 35 U.S.C. 102(b) rejection over Brana I (4204063) is withdrawn, because the amendment that the loweralkyl- R^5R^6 is $C_{2-4}alkylR^5R^6$ and the proviso that R^2 and R^3 are not both hydrogen have set a demarcation from the prior art compound.

9. The 35 U.S.C. 102(b) rejection over Brana II (J. Org. Chem., PTO-1449) is withdrawn because the amendment that the loweralkyl- R^5R^6 is $C_{2-4}alkylR^5R^6$ and the proviso that R^2 and R^3 are not both hydrogen have set a demarcation from the prior art compound.

Claim Rejections - 35 USC § 103

10. The 35 U.S.C. 103(a) rejection for claim 13 over Sestanj I (3821383, PTO-1449) in view of Bundgaard is withdrawn because the amendment that the loweralkyl- R^5R^6 is $C_{2-4}alkylR^5R^6$ and the proviso that R^2 and R^3 are not both hydrogen have set a demarcation from the prior art compound.

11. The 35 U.S.C. 103(a) rejection over Brana III (4874863, PTO-1449) is withdrawn in view of the amendment deleting the naphthalimide moiety from the definition of R^1 , thereby setting a demarcation from the prior art compound.

Double Patenting

12. The provisionally obviousness-type double patenting over the corresponding claims of copending Application No. 09/457606 is maintained for reasons of record. Applicant maintains that the present amendment has set a demarcation from the allowed claims of the copending application. The examiner may withdraw the rejection upon reviewing the allowed claims of the copending application.

Claim Rejections - 35 USC § 103

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

14. Claim 5 is rejected under 35 U.S.C. 103(a) as being unpatentable over Brana (4204063).

Brana generically discloses a naphthalimide with anti-tumor activity (column 1), and the pharmaceutical composition thereof. A specific compound is described (column 2, Example 3).

The prior art compound has an ethylene whereas the compound, 1,3-dioxo-5-nitro-N-propylmorpholino-1,2,3,4-tetrahydrobenzo[I]isoquinoline, of instant claim 5 has a propylene linking the morpholino and the naphthalimide nitrogen.

However, Brana teaches that ethylene and propylene are optional choices as the alkylene linkage in the anti-tumor compound (column 1, lines 30-32, definition of Y). the propylene linkage is exemplified (column 2, Example 5).

At the time of the invention, one of ordinary skill in the art would be motivated to prepare a pharmaceutical composition comprising a compound with the alternative propylene instead of ethylene in Brana's example compound to arrive at the instant invention with the reasonable expectation of obtaining a composition with anti-tumor activity.

15. Claim 5 is rejected under 35 U.S.C. 103(a) as being unpatentable over Sestanji I (3821383, PTO-1449).

Sestanji discloses a benzoisoquinoline compound useful for treating diabetic neuropathy. A specific compound, 5-nitro- 1,3-dioxo-1H-benz[de]isoquinoline-2(H)-acetic acid, is described (column 4, table).

Sestanji does not describe the ester of the example compound as in ethyl-5-nitro-1,3-dioxo-1-H-benze[de]isoquinoline-2-3H-acetate of the instant claim 5 .

However, ethyl ester are art-recognized prodrugs, which are expressly taught by Bundgaard (page 2, 27).

At the time of the invention, one of ordinary skill in the art would be motivated to prepare the composition comprising the ester prodrugs of Sestanji' compound as taught by Bundgaard to arrive at the instant invention with the reasonable expectation of enhancing the delivery of the drug compound.

16. Claims 1-6, 9-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sestanji I (3821383, PTO-1449) in view of Malizia (EP 206322, PTO-1449).

Sestanji discloses a benzoisoquinoline compound, and the composition thereof, useful for treating diabetic neuropathy. A specific compound, 5-nitro-1,3-dioxo-1H-benz[de]isoquinoline-2(H)-acetic acid, is described (column 4, table).

Sestanji's compound has an acetic acid moiety whereas the compound, 3-nitro-1,8-(N-propioncarboxylate) succinamidonaphthalene of the instant claims 5, 6 has a propionic acid moiety. The instant propionic acid is therefore the next adjacent homolog of Sestanji's acetic acid.

Malizia specifically teaches that compound I, the propionic acid homolog of Sestanji's compound, is more active and endowed with more advantageous pharmaco-therapeutics characteristics (page 2, lines 12-19).

At the time of the invention, one of ordinary skill in the art would be motivated to prepare the composition comprising the more active propionic acid compound as taught by Malizia in place of Sestanji' acetic acid compound to arrive at the instant invention with the reasonable expectation of obtaining a more effective composition for treatment of neuropathy.

17. Claim 13 is rejected under 35 U.S.C. 103(a) as being unpatentable over Sestanji I (3821383, PTO-1449) in view of Malizia (EP 206322, PTO-1449) for reasons set forth in the above paragraph and further in view of Bundgaard.

Sestanji or Malizia does not describe the ester or amide of the compound as in the instant 3-nitro-1,8-(N-propioncarboxylate) succinamidonaphthalene.

However, ester and amide are art-recognized prodrugs, which are expressly taught by Bundgaard (page 2, 27).

At the time of the invention, one of ordinary skill in the art would be motivated to prepare the ester and amide prodrugs of 3-nitro-1,8-(N-propioncarboxylate) succinamidonaphthalene as taught by Bundgaard to arrive at the instant invention with the reasonable expectation of a composition with enhanced delivery of the drug compound.

Claim Rejections - 35 USC § 112

18. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 5, 6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claim 5, some of the compounds, such as 2-{2-(4-methylphenyl-sulphon-amido)-5,5-dichlorophenyl}-naphthalimide (wherein R2 and R3 are both hydrogen), 1,3-dioxo-5-nitro-N-propylmorpholino-1,2,3,4-tetrahydrobenzo[I]isoquinoline, 5-amino-N-butyl naphthalimide etc., have no antecedent basis in the base claim 1.

b. Claim 6, some of the compounds, such as 2-{2-(4-methylphenyl-sulphonamido)-5,5-dichlorophenyl}-naphthalimide (wherein R2 and R3 are both hydrogen), have no antecedent basis in the base claim 2.

Allowable Subject Matter

19. Claim 7 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

The composition comprising a compound wherein R1 is aminoethanol as recited in the instant claim is not taught or suggested by all of the prior art of the preceding paragraphs.

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Conclusion

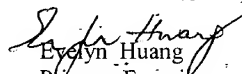
20. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

21. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Evelyn Huang whose telephone number is 703-305-7247. The examiner can normally be reached on Tuesday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Alan Rotman can be reached on 703-308-4698. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4556 for regular communications and 703-308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.


Evelyn Huang
Primary Examiner
Art Unit 1625

September 24, 2002